

# Probabilities of Death From Breast Cancer and Other Causes Among Female Breast Cancer Patients

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**Background:** Among cancer patients, probabilities of death from that cancer and other causes in the presence of competing risks are optimal measures of prognosis and of mortality across demographic groups. We used data on breast cancer patients from the Surveillance, Epidemiology, and End Results (SEER) Program in a competing-risk analysis. **Methods:** We determined vital status and cause of death for 395 251 white and 35 259 black female patients with breast cancer diagnosed from January 1, 1973, through December 31, 2000, by use of SEER data. We calculated probabilities of death from breast cancer and other causes according to stage, race, and age at diagnosis; for cases diagnosed from January 1, 1990, to December 31, 2000, we also calculated some such probabilities according to tumor size and estrogen receptor (ER) status. All statistical tests were two-sided. **Results:** The probability of death from breast cancer after nearly 28 years of follow-up ranged from 0.03 to 0.10 for patients with *in situ* disease to 0.70 to 0.85 for patients with distant disease, depending on race and age. The probability of death from breast cancer at the end of the follow-up period generally declined with age at diagnosis; the probability among the oldest ( $\geq 70$  years) compared with the youngest ( $< 50$  years) patients was 33% lower for white and 46% lower for black patients with localized disease and 14% lower for white patients and 13% lower for black patients with distant disease. The probability of death from breast cancer exceeded that from all other causes for patients diagnosed with localized disease before age 50 years, with regional disease before age 60 years, and with distant disease at any age. The probability of death from breast cancer for patients diagnosed with localized or regional disease was statistically significantly greater in black patients than in white patients (all six  $P$  values  $\leq .01$  for age groups 30–49 to 60–69 years; two  $P$  values  $\leq .04$  for ages  $\geq 70$  years). Among patients with localized or regional disease and known ER status, the probability of death from breast cancer after nearly 11 years of follow-up ranged from 0.04 to 0.11 for patients with localized ER-positive tumors of 2 cm or less to 0.37 to 0.53 for patients with regional ER-negative tumors. **Conclusions:** The probability of death from breast cancer versus other causes varied substantially according to stage, tumor size, ER status, and age at diagnosis in both white and black patients. [J Natl Cancer Inst 2004;96:1311–21]

Relative survival, which is the ratio of the observed survival rate to the expected survival rate derived from mortality rates for the general population, is frequently used as a measure of cause-specific mortality in the absence of other causes of death (1). The 5-year relative survival after a diagnosis of breast

cancer has been lower in black patients than in white patients and also slightly lower in younger patients ( $< 65$  years) than in older patients ( $\geq 65$  years) (1). However, relative survival is not influenced by competing causes of death, cannot be partitioned into cause-specific categories, and does not reflect the mortality patterns actually observed (2). Because comorbidity from competing causes increases with advancing age (3) and is greater in black patients than in white patients (4,5), relative survival may not be the optimal measure for assessing the impact of a breast cancer diagnosis at an individual level or for comparing mortality across racial and/or age groups (2).

Crude cumulative cause-specific probabilities of death that are based on a competing-risk model provide measures of cause-specific mortality in the presence of other causes of death and reflect the mortality patterns actually observed (2). Thus, they are the optimal measures of prognosis after a cancer diagnosis. Among patients with breast cancer, such probabilities would be especially useful in weighing the risks and benefits of various treatment options, particularly in patients diagnosed at older ages, when comorbidity is high (6). In fact, comorbidity in breast cancer patients limits treatment options, increases the risk of death from other causes (3,7), and adversely affects survival (3,8–10). Cumulative cause-specific probabilities are also ideal for assessing mortality across racial and/or age groups. In a competing-risk analysis of breast cancer mortality in patients with regional breast cancer, the cumulative probability of death from breast cancer declined as age increased because of the increasing risk of death from other causes (2). However, this analysis did not provide data for other stages of disease, did not account for race, and did not include the probability of death from other causes.

To develop improved prognostic information and to assess the burden of mortality from breast cancer and other causes by age and race, we used the theory of competing risks to calculate crude cumulative probabilities of death from breast cancer and other causes in female patients with breast cancer according to stage, race, age, and, for a subset of analyses, tumor size and estrogen receptor (ER) status. We used Surveillance, Epidemiology, and End Results (SEER)<sup>1</sup> data for cases of breast cancer diagnosed from January 1, 1973, through December 31, 2000.

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## PATIENTS AND METHODS

### Patients

Using data from the SEER Program, we identified 402 082 white patients (non-Hispanic and Hispanic) and 35 933 black patients diagnosed with *in situ* or invasive breast cancer from January 1, 1973, through December 31, 2000, in nine SEER registries (states of Connecticut, Iowa, New Mexico, Utah, and Hawaii, and the metropolitan areas of Detroit, Atlanta, San Francisco–Oakland Standard Metropolitan Statistical Area, and Seattle [Puget Sound]) and from January 1, 1992, through December 31, 2000, in two additional SEER registries (San Jose–Monterey and Los Angeles). We included only the first diagnosis of breast cancer recorded by the SEER Program for each patient. We excluded 7505 of these cases for the following reasons: no follow-up time ( $n = 4731$ ), errors in cause-of-death codes ( $n = 36$ ), and breast cancer first identified on death certificate or by autopsy ( $n = 2738$ ). After all exclusions, data from 395 251 white patients and 35 259 black patients were available for analysis. We omitted the 29 245 cases among patients of other and unknown races.

Case records were followed for vital status until the earliest of the following dates: death; last contact if before December 31, 2000; or December 31, 2000, if date of last contact was after 2000. We grouped causes of death into two groups: death from breast cancer (International Classification of Diseases [ICD]-8 or ICD-9 code = 174; ICD-10 = C50) and death from all other causes, including unknown causes. Among deaths from all other causes, 33% were attributed to heart disease, 20% to cancers other than breast cancer, 11% to circulatory disease, 9% to diseases of the respiratory system, and 26% to other or unknown causes. We categorized women according to race (white or black), age at diagnosis (<50, 50–59, 60–69, or  $\geq 70$  years), and SEER historic stage A, a staging scheme used by SEER to classify cases as *in situ*, localized, regional, distant, or unstaged (11). Localized disease pertains to malignant tumor confined to the breast tissue and fat, including the nipple and/or areola. Regional disease pertains to tumor that has extended beyond the limits of the breast directly into surrounding organs or tissues, tumor that involves regional lymph nodes by way of the lymphatic system, or tumor that has regional extension and involvement of regional lymph nodes. Distant disease refers to malignant neoplasms that have spread to parts of the body that are remote from the breast either by direct extension or by discontinuous metastasis to distant organs, tissues, or via the lymphatic system to distant lymph nodes. We used this staging scheme because it was available for the entire period from January 1, 1973, through December 31, 2000. We classified patients with synchronous bilateral breast cancer according to their most advanced stage.

Information on both tumor size (SEER Extent of Disease code for size) and ER status was available for cases diagnosed from January 1, 1990, through December 31, 2000. We categorized cases with localized disease diagnosed during these years by tumor size ( $\leq 2$  cm,  $> 2$  cm, or unknown) and ER status (positive, negative, or other). We included those with a SEER Extent of Disease size code of 002 (mammography/xerography diagnosis only with no size given or tumor not clinically palpable) in the smaller-size group and those with a code of 998 (diffuse, widespread, three-fourths or more of breast, or inflam-

matory carcinoma) in the larger-size group. Those with a size code of 997 (Paget disease of nipple with no demonstrable tumor) or a size code of 999 (unknown) were included in the unknown-size category. Among 121 389 white patients and 9967 black patients diagnosed with localized disease between January 1, 1990, and December 31, 2000, the tumor size was known for 95% (115 038) of white patients and 93% (9318) of black patients. ER status was known for 81% (92 744) of white patients and 74% (6890) of black patients with localized disease and known tumor size. We also classified those with regional disease according to ER status, which was available for 83% (45 433) of 54 824 white patients and 77% (5024) of 6547 black patients.

### Statistical Analysis

We calculated crude cumulative probabilities of death by time since diagnosis (in months) for breast cancer and other causes in the presence of competing risks by stage, race, and age at diagnosis and, for a subset of analyses, by tumor size and ER status. We used software developed by Gooley et al. (12). Statistics based on cumulative weighted differences and accompanying *P* values were used to compare the cumulative probabilities of death from breast cancer and other causes in white patients and black patients, via software developed by Pepe et al. (13). Differences at later time points, for which the number of subjects under observation was smaller because of censoring, were weighted less heavily in these functions (13). The preset level of statistical significance was 5% from a two-sided statistical test. All statistical tests were two-sided.

## RESULTS

The SEER program recorded 395 251 cases of breast cancer in white women and 35 259 cases of breast cancer in black women diagnosed from January 1, 1973, through December 31, 2000. Among white patients, 10.8% had tumors that were *in situ* at diagnosis, 51.9% had tumors that were localized to the breast, 29.4% had regional metastases, 5.1% had distant metastases, and 2.9% were unstaged (Table 1). Among black patients, the corresponding percentages were 11.4, 43.3, 33.5, 8.0, and 3.8%. The follow-up time ranged from 1 month to 27.9 years, corresponding to the duration of the SEER program database. The mean duration of follow-up among white patients was 8.0 years in those aged younger than 50 years at diagnosis, 7.7 years in those aged 50–59 years, 7.5 years in those aged 60–69 years, and 5.3 years in those aged 70 years and older. The corresponding mean durations among black patients were 6.4, 5.9, 5.8, and 4.5 years.

Among white patients after nearly 28 years of follow-up, the probabilities of death from breast cancer at the end of the follow-up period ranging by age within stage were 0.04 to 0.05, 0.14 to 0.21, 0.34 to 0.49, and 0.70 to 0.81 for *in situ*, localized, regional, and distant disease, respectively (Table 1). The corresponding probabilities among black patients were 0.03 to 0.10, 0.15 to 0.28, 0.42 to 0.55, and 0.72 to 0.85.

Among patients diagnosed with *in situ* disease, the probability of death from other causes exceeded that for breast cancer at all ages at diagnosis (Table 1). The probability of death from breast cancer was not statistically significantly different in white patients and black patients.

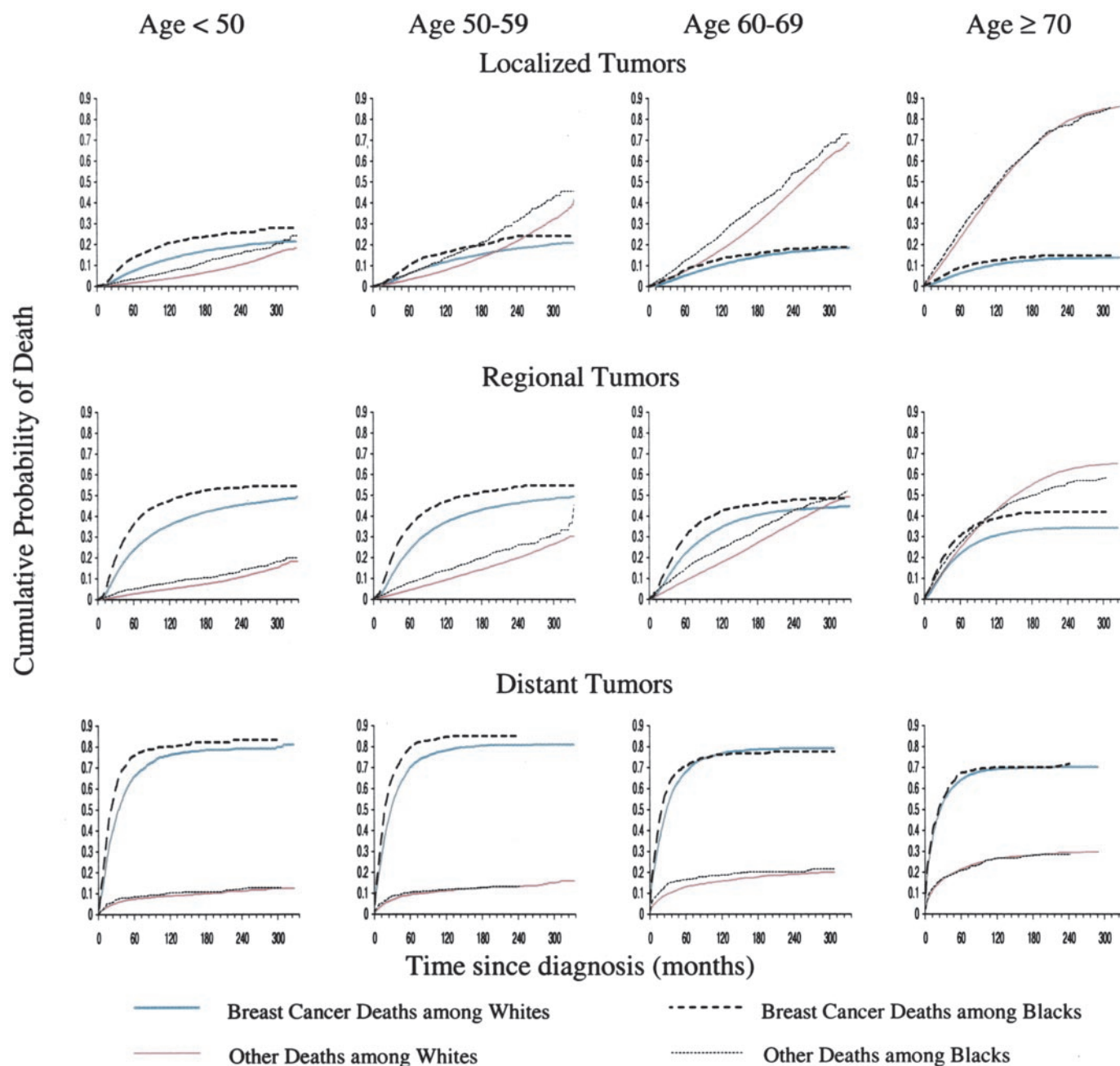
**Table 1.** Number of breast cancer cases, deaths from breast cancer and other causes, and cumulative probabilities of death from breast cancer and other causes according to stage, race, and age (in years) at diagnosis: Surveillance, Epidemiology, and End Results (SEER) Program, 1973–2000

| Category                 | No. of breast cancer cases | No. of breast cancer deaths | Probability of death from breast cancer 5 y after diagnosis | Probability of death from breast cancer at end of follow-up (27.9 y) | No. of other deaths | Probability of death from other causes 5 y after diagnosis | Probability of death from other causes at end of follow-up (27.9 y) |
|--------------------------|----------------------------|-----------------------------|---|--|---------------------|--|---|
| <i>In situ disease</i>   |                            |                             |   |  |                     |  |   |
| White patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 12 143                     | 115                         | 0.004   | 0.04   | 276                 | 0.01   | 0.20  |
| 50–59 y                  | 10 893                     | 92                          | 0.004   | 0.04   | 494                 | 0.02   | 0.37  |
| 60–69 y                  | 9566                       | 113                         | 0.006   | 0.04   | 1094                | 0.05   | 0.71  |
| ≥70 y                    | 10 130                     | 172                         | 0.01  | 0.05   | 2556                | 0.16   | 0.94  |
| Black patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 1275                       | 20                          | 0.01  | 0.05   | 48                  | 0.02   | 0.29  |
| 50–59 y                  | 980                        | 12                          | 0.01  | 0.07   | 72                  | 0.06   | 0.44  |
| 60–69 y                  | 867                        | 11                          | 0.01  | 0.03   | 128                 | 0.10   | 0.81  |
| ≥70 y                    | 901                        | 25                          | 0.02  | 0.10   | 260                 | 0.19   | 0.90  |
| <i>Localized disease</i> |                            |                             |   |  |                     |  |   |
| White patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 41 363                     | 4580                        | 0.07  | 0.21   | 1916                | 0.02   | 0.18  |
| 50–59 y                  | 41 044                     | 4080                        | 0.06  | 0.21   | 4039                | 0.03   | 0.42  |
| 60–69 y                  | 49 590                     | 4589                        | 0.05  | 0.18   | 10 300              | 0.07   | 0.69  |
| ≥70 y                    | 72 997                     | 5975                        | 0.06  | 0.14   | 29 254              | 0.23   | 0.86  |
| Black patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 4847                       | 776                         | 0.13  | 0.28   | 330                 | 0.03   | 0.24  |
| 50–59 y                  | 3372                       | 415                         | 0.10  | 0.24   | 427                 | 0.06   | 0.45  |
| 60–69 y                  | 3345                       | 340                         | 0.08  | 0.19   | 782                 | 0.12   | 0.72  |
| ≥70 y                    | 3705                       | 349                         | 0.09  | 0.15   | 1427                | 0.26   | 0.85  |
| <i>Regional disease</i>  |                            |                             |   |  |                     |  |   |
| White patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 30 343                     | 9217                        | 0.24  | 0.49   | 1741                | 0.03   | 0.18  |
| 50–59 y                  | 26 368                     | 8526                        | 0.23  | 0.49   | 3073                | 0.04   | 0.30  |
| 60–69 y                  | 26 313                     | 8382                        | 0.22  | 0.44   | 5852                | 0.09   | 0.49  |
| ≥70 y                    | 33 074                     | 8831                        | 0.22  | 0.34   | 13 622              | 0.25   | 0.65  |
| Black patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 4407                       | 1694                        | 0.36  | 0.54   | 330                 | 0.05   | 0.20  |
| 50–59 y                  | 2805                       | 1076                        | 0.35  | 0.55   | 392                 | 0.08   | 0.45  |
| 60–69 y                  | 2354                       | 835                         | 0.30  | 0.48   | 590                 | 0.14   | 0.52  |
| ≥70 y                    | 2253                       | 739                         | 0.30  | 0.42   | 827                 | 0.27   | 0.58  |
| <i>Distant disease</i>   |                            |                             |   |  |                     |  |   |
| White patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 3561                       | 2286                        | 0.66  | 0.81   | 285                 | 0.07   | 0.13  |
| 50–59 y                  | 4173                       | 2848                        | 0.70  | 0.81   | 438                 | 0.09   | 0.16  |
| 60–69 y                  | 5267                       | 3716                        | 0.68  | 0.79   | 818                 | 0.13   | 0.20  |
| ≥70 y                    | 7157                       | 4586                        | 0.64  | 0.70   | 1756                | 0.21   | 0.30  |
| Black patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 817                        | 574                         | 0.76  | 0.83   | 71                  | 0.08   | 0.13  |
| 50–59 y                  | 626                        | 476                         | 0.79  | 0.85   | 68                  | 0.10   | 0.13  |
| 60–69 y                  | 656                        | 464                         | 0.70  | 0.77   | 117                 | 0.16   | 0.21  |
| ≥70 y                    | 714                        | 456                         | 0.67  | 0.72   | 162                 | 0.21   | 0.28  |
| <i>Unknown stage</i>     |                            |                             |   |  |                     |  |   |
| White patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 2068                       | 847                         | 0.26  | 0.54   | 209                 | 0.04   | 0.19  |
| 50–59 y                  | 1691                       | 712                         | 0.27  | 0.54   | 288                 | 0.07   | 0.29  |
| 60–69 y                  | 2042                       | 880                         | 0.27  | 0.53   | 597                 | 0.13   | 0.44  |
| ≥70 y                    | 5468                       | 2070                        | 0.31  | 0.42   | 2649                | 0.36   | 0.58  |
| Black patients           |                            |                             |   |  |                     |  |   |
| <50 y                    | 345                        | 161                         | 0.44  | 0.65   | 30                  | 0.07   | 0.19  |
| 50–59 y                  | 237                        | 109                         | 0.36  | 0.61   | 47                  | 0.15   | 0.39  |
| 60–69 y                  | 233                        | 101                         | 0.33  | 0.57   | 59                  | 0.18   | 0.33  |
| ≥70 y                    | 520                        | 181                         | 0.31  | 0.42   | 239                 | 0.39   | 0.58  |

Among both white patients and black patients with localized disease (Table 1 and Fig. 1), death from breast cancer was the predominant cause of death over the entire study period for women diagnosed before age 50 years. For those diagnosed between ages 50 and 59 years, it was the predominant cause of death for at least 17 years after diagnosis in white patients and for 13 years after diagnosis in black patients. At older ages, the probability of death from other causes became increasingly important. The cumulative probability of death from breast cancer by the end of the study period generally declined with increasing age at diagnosis; the probability in the oldest ( $\geq 70$  years) compared with the youngest ( $<50$  years) patients was 33% [(0.21 - 0.14)/0.21] lower in white patients and 46% [(0.28 - 0.15)/0.28] lower in black patients. The probability of death

from breast cancer was statistically significantly greater in black patients than white patients diagnosed at all ages ( $P \leq .001$  for ages 30–49 years,  $P \leq .001$  for ages 50–59 years,  $P = .008$  for ages 60–69 years, and  $P = .04$  for ages  $\geq 70$  years), but the differences decreased with advancing age. The probability of death from other causes was statistically significantly greater in black patients than in white patients diagnosed before age 70 years ( $P \leq .001$  for ages 30–49 years,  $P \leq .001$  for ages 50–59 years, and  $P \leq .001$  for ages 60–69 years).

For white patients and black patients with regional disease (Table 1 and Fig. 1), breast cancer was the predominant cause of death for the entire follow-up period in those diagnosed before age 60 years and for nearly the entire follow-up period for those diagnosed at ages 60–69 years. Among women diagnosed at age



**Fig. 1.** Cumulative probability of death from breast cancer and other causes according to stage, race, and age at diagnosis (in years), Surveillance, Epidemiology, and End Results (SEER) Program, 1973–2000.



70 years or older, the probabilities of death from breast cancer and other causes were similar for the first 4 years after diagnosis in white patients and for 7 years after diagnosis in black patients, after which time the probability of death from other causes predominated in both black patients and white patients. The greatest increases in breast cancer mortality occurred within the first 5 years of diagnosis. The probability of death from breast cancer at the end of the study period declined with increasing age at diagnosis; the probability in the oldest ( $\geq 70$  years) compared with the youngest ( $< 50$  years) patients was 31% lower in white patients and 22% lower in black patients. Over the follow-up period, the probability of death from breast cancer was statistically significantly greater in black patients than in white patients at all ages ( $P \leq .001$  for ages 30–49 years,  $P \leq .001$  for ages 50–59 years,  $P = .003$  for ages 60–69 years, and  $P = .02$  for ages  $\geq 70$  years). The probability of death from other causes was statistically significantly greater in black patients than in white patients diagnosed before age 70 years ( $P \leq .001$  for ages 30–49 years,  $P \leq .001$  for ages 50–59 years, and  $P \leq .001$  for ages 60–69 years).

Among white patients and black patients with distant metastases (Table 1 and Fig. 1), death from breast cancer was the overwhelming cause of death regardless of age at diagnosis, with most deaths occurring within the first 5 years of diagnosis. The probability of death from breast cancer at the end of the follow-up period for the oldest ( $\geq 70$  years) compared with the youngest ( $< 50$  years) patients was 14% lower in white patients and 13% lower in black patients. The probability of death from breast cancer was not statistically significantly different in white patients and black patients.

Among both white patients and black patients, the percentages of deaths from heart disease and circulatory disease increased with age, whereas those for cancers other than breast cancer declined, as did those from other causes (Table 2). Among white patients, but not black patients, the percentage of deaths attributed to respiratory disease increased with age.

We did further analyses among those with localized disease according to tumor size and ER status for cases of breast cancer diagnosed from January 1, 1990, through December 31, 2000 (Table 3 and Fig. 2). The minimum and maximum follow-up times were 1 month and 10.9 years, respectively, with the mean ranging from 3.7 years in black patients aged 70 years and older

at diagnosis to 4.8 years in white patients aged 60–69 years at diagnosis. Among white patients with tumors of 2 cm or less in diameter, the probability of death from breast cancer at the end of the follow-up period was 0.04 to 0.07 for patients with ER-positive tumors and 0.09 to 0.10 for patients with ER-negative tumors, depending on age; the corresponding probabilities for patients with tumors of more than 2 cm in diameter were 0.13 to 0.15 and 0.16 to 0.23. Among black patients, the probability of death from breast cancer ranged from 0.06 to 0.11 for patients with ER-positive tumors of 2 cm or less in diameter to 0.19 to 0.28 for patients with ER-negative tumors of more than 2 cm in diameter.

For patients diagnosed with localized disease, the probability of death from breast cancer was greater than that from all other causes for white patients and black patients diagnosed before age 50 years with ER-positive tumors of 2 cm or less in diameter, for white patients diagnosed before age 60 years and black patients before age 50 years with ER-negative tumors of 2 cm or less in diameter, for white patients and black patients diagnosed before age 60 years with ER-positive tumors of more than 2 cm, and for white patients and black patients diagnosed before age 70 years with ER-negative tumors of more than 2 cm (Table 3 and Fig. 2). The probability of death from breast cancer was statistically significantly greater in black patients than in white patients diagnosed with ER-negative tumors before age 50 years ( $P = .008$  for tumors  $\leq 2$  cm and  $P = .003$  for tumors  $> 2$  cm), with ER-positive tumors of 2 cm or less in diameter between ages 50 years and 59 years ( $P = .03$ ), or with ER-positive tumors of more than 2 cm at ages 70 years or older ( $P = .01$ ).

Analyses for patients with regional disease according to ER status are shown in Table 4 and Fig. 3. Follow-up time for patients diagnosed with regional disease from January 1, 1990, to December 31, 2000, ranged from 1 month to 10.9 years, with the mean ranging from 3.1 years to 4.3 years, depending on age and race. Among white patients with regional disease, the probability of death from breast cancer at the end of the follow-up period was 0.23 to 0.25 in those with ER-positive tumors and 0.37 to 0.43 in those with ER-negative tumors, depending on age. The corresponding probabilities among black patients were 0.34 to 0.44 and 0.43 to 0.53. Breast cancer was the predominant cause of death among white patients and black patients with ER-positive disease diagnosed before age 70 years and ER-

**Table 2.** Number and percentage of deaths from causes other than breast cancer by age at breast cancer diagnosis and race for all stages combined: Surveillance, Epidemiology, and End Results (SEER) Program, 1973–2000

| Category                      | Heart disease,<br>No. (%) | Cancers other than<br>breast cancer,<br>No. (%) | Circulatory disease,<br>No. (%) | Respiratory disease,<br>No. (%) | Other disease,<br>No. (%) | Total<br>No. (%) |
|-------------------------------|---------------------------|---|---------------------------------|---------------------------------|---------------------------|------------------|
| <b>&lt;50 y</b>               |                           |   |                                 |                                 |                           |                  |
| White patients                | 556 (12.6)                | 1558 (35.2)                                     | 139 (3.1)                       | 249 (5.6)                       | 1925 (43.5)               | 4427 (100)       |
| Black patients                | 135 (16.7)                | 216 (26.7)                                      | 37 (4.6)                        | 45 (5.6)                        | 376 (46.5)                | 809 (100)        |
| <b>50–59 y</b>                |                           |   |                                 |                                 |                           |                  |
| White patients                | 1823 (21.9)               | 2703 (32.4)                                     | 489 (5.9)                       | 689 (8.3)                       | 2628 (31.5)               | 8332 (100)       |
| Black patients                | 295 (29.3)                | 262 (26.0)                                      | 75 (7.5)                        | 49 (4.9)                        | 325 (32.3)                | 1006 (100)       |
| <b>60–69 y</b>                |                           |   |                                 |                                 |                           |                  |
| White patients                | 5408 (29.0)               | 4853 (26.0)                                     | 1686 (9.0)                      | 1795 (9.6)                      | 4919 (26.4)               | 18 661 (100)     |
| Black patients                | 573 (34.2)                | 358 (21.4)                                      | 147 (8.8)                       | 119 (7.1)                       | 479 (28.6)                | 1676 (100)       |
| <b><math>\geq 70</math> y</b> |                           |   |                                 |                                 |                           |                  |
| White patients                | 19 373 (38.9)             | 6879 (13.8)                                     | 7044 (14.1)                     | 4939 (9.9)                      | 11 602 (23.3)             | 49 837 (100)     |
| Black patients                | 1130 (38.8)               | 455 (15.6)                                      | 368 (12.6)                      | 170 (5.8)                       | 792 (27.2)                | 2915 (100)       |

**Table 3.** Number of breast cancer cases with localized disease, deaths from breast cancer and other causes, and cumulative probabilities of death from breast cancer and other causes according to tumor size, estrogen receptor (ER) status, race, and age (in years) at diagnosis: Surveillance, Epidemiology, and End Results (SEER) Program, 1990–2000

| Category*                      | No. of breast cancer cases | No. of breast cancer deaths | Probability of death from breast cancer 5 y after diagnosis | Probability of death from breast cancer at end of follow-up (10.9 y) | No. of other deaths | Probability of death from other causes 5 y after diagnosis | Probability of death from other causes at end of follow-up (10.9 y) |
|--------------------------------|----------------------------|-----------------------------|---|--|---------------------|--|---|
| <b>Tumors ≤2 cm and ER+</b>    |                            |                             |   |  |                     |  |   |
| White patients                 |                            |                             |   |  |                     |  |   |
| <50 y                          | 9406                       | 194                         | 0.02  | 0.07   | 112                 | 0.01   | 0.04  |
| 50–59 y                        | 11 764                     | 149                         | 0.01  | 0.04   | 269                 | 0.03   | 0.07  |
| 60–69 y                        | 14 891                     | 299                         | 0.02  | 0.06   | 1023                | 0.06   | 0.18  |
| ≥70 y                          | 23 206                     | 621                         | 0.03  | 0.06   | 4491                | 0.19   | 0.50  |
| Black patients                 |                            |                             |   |  |                     |  |   |
| <50 y                          | 714                        | 24                          | 0.03  | 0.11   | 17                  | 0.03   | 0.07  |
| 50–59 y                        | 684                        | 17                          | 0.04  | 0.06   | 17                  | 0.03   | 0.09  |
| 60–69 y                        | 803                        | 22                          | 0.04  | 0.06   | 82                  | 0.11   | 0.29  |
| ≥70 y                          | 965                        | 34                          | 0.04  | 0.07   | 210                 | 0.25   | 0.50  |
| <b>Tumors ≤2 cm and ER–</b>    |                            |                             |   |  |                     |  |   |
| White patients                 |                            |                             |   |  |                     |  |   |
| <50 y                          | 3505                       | 181                         | 0.06  | 0.09   | 54                  | 0.01   | 0.05  |
| 50–59 y                        | 2931                       | 144                         | 0.06  | 0.09   | 76                  | 0.03   | 0.06  |
| 60–69 y                        | 2606                       | 136                         | 0.06  | 0.09   | 199                 | 0.07   | 0.15  |
| ≥70 y                          | 3059                       | 196                         | 0.07  | 0.10   | 583                 | 0.19   | 0.46  |
| Black patients                 |                            |                             |   |  |                     |  |   |
| <50 y                          | 539                        | 46                          | 0.10  | 0.15   | 21                  | 0.04   | 0.08  |
| 50–59 y                        | 365                        | 21                          | 0.08  | 0.10   | 21                  | 0.08   | 0.15  |
| 60–69 y                        | 295                        | 24                          | 0.08  | 0.13   | 33                  | 0.12   | 0.25  |
| ≥70 y                          | 238                        | 18                          | 0.08  | 0.14   | 52                  | 0.25   | 0.45  |
| <b>Tumors &gt;2 cm and ER+</b> |                            |                             |   |  |                     |  |   |
| White patients                 |                            |                             |   |  |                     |  |   |
| <50 y                          | 2911                       | 187                         | 0.07  | 0.14   | 46                  | 0.02   | 0.03  |
| 50–59 y                        | 2644                       | 146                         | 0.06  | 0.15   | 85                  | 0.04   | 0.11  |
| 60–69 y                        | 3020                       | 194                         | 0.06  | 0.13   | 281                 | 0.09   | 0.27  |
| ≥70 y                          | 6519                       | 461                         | 0.07  | 0.13   | 1810                | 0.29   | 0.56  |
| Black patients                 |                            |                             |   |  |                     |  |   |
| <50 y                          | 347                        | 30                          | 0.11  | 0.17   | 5                   | 0.02   | 0.03  |
| 50–59 y                        | 247                        | 17                          | 0.08  | 0.15   | 13                  | 0.05   | 0.11  |
| 60–69 y                        | 236                        | 13                          | 0.06  | 0.18   | 34                  | 0.14   | 0.25  |
| ≥70 y                          | 372                        | 40                          | 0.14  | 0.17   | 103                 | 0.30   | 0.58  |
| <b>Tumors &gt;2 cm and ER–</b> |                            |                             |   |  |                     |  |   |
| White patients                 |                            |                             |   |  |                     |  |   |
| <50 y                          | 2415                       | 251                         | 0.13  | 0.16   | 53                  | 0.03   | 0.05  |
| 50–59 y                        | 1405                       | 182                         | 0.17  | 0.21   | 55                  | 0.04   | 0.10  |
| 60–69 y                        | 1031                       | 154                         | 0.18  | 0.23   | 108                 | 0.10   | 0.22  |
| ≥70 y                          | 1431                       | 216                         | 0.18  | 0.23   | 360                 | 0.26   | 0.53  |
| Black patients                 |                            |                             |   |  |                     |  |   |
| <50 y                          | 497                        | 75                          | 0.19  | 0.23   | 17                  | 0.03   | 0.08  |
| 50–59 y                        | 289                        | 48                          | 0.23  | 0.27   | 24                  | 0.08   | 0.17  |
| 60–69 y                        | 155                        | 25                          | 0.17  | 0.28   | 16                  | 0.11   | 0.19  |
| ≥70 y                          | 144                        | 21                          | 0.17  | 0.19   | 36                  | 0.27   | 0.50  |

\*ER+ = ER positive; ER– = ER negative.

negative disease diagnosed at all ages. The probability of death from breast cancer was statistically significantly greater in black patients than in white patients diagnosed with ER-positive tumors at all ages ( $P \leq .001$  for ages 30–49 years;  $P \leq .001$  for ages 50–59 years;  $P \leq .001$  for ages 60–69 years; and  $P = .003$  for ages ≥70 years) or with ER-negative disease before the age of 70 years ( $P \leq .001$  for ages 30–49 years;  $P \leq .001$  for ages 50–59 years; and  $P = .001$  for ages 60–69 years).

In analyses of patients 70 years and older at diagnosis, death from breast cancer accounted for 6% of the total probability of

death 5 years after diagnosis among white patients with *in situ* disease (total probability of death [0.17] = probability of death from breast cancer [0.01] + probability of death from other causes [0.16]; derived from Table 1). For white patients, this percentage was 14% among patients with localized ER-positive tumors 2 cm or less in diameter, 19% among patients with localized ER-positive tumors of greater than 2 cm in diameter, 27% among patients with localized ER-negative tumors of 2 cm or less in diameter, 41% among patients with localized ER-negative tumors of more than 2 cm in diameter

**Table 4.** Number of breast cancer cases with regional disease, deaths from breast cancer and other causes, and cumulative probabilities of death from breast cancer and other causes according to estrogen receptor (ER) status, race, and age (in years) at diagnosis: Surveillance, Epidemiology, and End Results (SEER) Program, 1990–2000

| Category*      | No. of breast cancer cases | No. of breast cancer deaths | Probability of death from breast cancer 5 y after diagnosis | Probability of death from breast cancer at end of follow-up (10.9 y) | No. of other deaths | Probability of death from other causes 5 y after diagnosis | Probability of death from other causes at end of follow-up (10.9 y) |
|----------------|----------------------------|-----------------------------|---|--|---------------------|--|---|
| <b>ER+</b>     |                            |                             |   |  |                     |  |   |
| White patients |                            |                             |   |  |                     |  |   |
| <50 y          | 9001                       | 1015                        | 0.13  | 0.25   | 194                 | 0.02   | 0.05  |
| 50–59 y        | 7713                       | 824                         | 0.12  | 0.25   | 273                 | 0.04   | 0.12  |
| 60–69 y        | 7384                       | 931                         | 0.13  | 0.24   | 632                 | 0.08   | 0.19  |
| ≥70 y          | 10 421                     | 1420                        | 0.15  | 0.23   | 2406                | 0.23   | 0.51  |
| Black patients |                            |                             |   |  |                     |  |   |
| <50 y          | 1039                       | 203                         | 0.23  | 0.44   | 27                  | 0.03   | 0.04  |
| 50–59 y        | 684                        | 120                         | 0.20  | 0.36   | 37                  | 0.06   | 0.10  |
| 60–69 y        | 597                        | 107                         | 0.21  | 0.34   | 68                  | 0.12   | 0.28  |
| ≥70 y          | 678                        | 127                         | 0.23  | 0.37   | 161                 | 0.24   | 0.49  |
| <b>ER–</b>     |                            |                             |   |  |                     |  |   |
| White patients |                            |                             |   |  |                     |  |   |
| <50 y          | 4243                       | 1031                        | 0.29  | 0.37   | 117                 | 0.03   | 0.06  |
| 50–59 y        | 2565                       | 584                         | 0.28  | 0.37   | 99                  | 0.04   | 0.09  |
| 60–69 y        | 1924                       | 507                         | 0.31  | 0.39   | 169                 | 0.09   | 0.16  |
| ≥70 y          | 2182                       | 683                         | 0.36  | 0.43   | 431                 | 0.21   | 0.38  |
| Black patients |                            |                             |   |  |                     |  |   |
| <50 y          | 970                        | 328                         | 0.41  | 0.50   | 43                  | 0.05   | 0.07  |
| 50–59 y        | 499                        | 159                         | 0.42  | 0.46   | 39                  | 0.09   | 0.18  |
| 60–69 y        | 316                        | 108                         | 0.43  | 0.53   | 27                  | 0.09   | 0.16  |
| ≥70 y          | 241                        | 81                          | 0.42  | 0.43   | 53                  | 0.24   | 0.34  |

\*ER+ = ER positive; ER– = ER negative.

(Table 3), 39% among patients with regional ER-positive tumors, 63% among patients with regional ER-negative tumors (Table 4), and 75% among patients with distant disease (Table 1). For black patients, the corresponding percentages were 10% among patients with *in situ* disease (Table 1), 14% among patients with localized ER-positive tumors 2 cm or less in diameter, 32% among patients with localized ER-positive tumors of more than 2 cm in diameter, 24% among patients with localized ER-negative tumors of 2 cm or less in diameter, 39% among patients with localized ER-negative tumors greater than 2 cm in diameter (Table 3), 49% among patients with regional ER-positive tumors, 64% among patients with regional ER-negative tumors (Table 4), and 76% among patients with distant disease (Table 1). The percentage of the total probability of death accounted for by breast cancer tended to decline with time since diagnosis among both white patients and black patients.

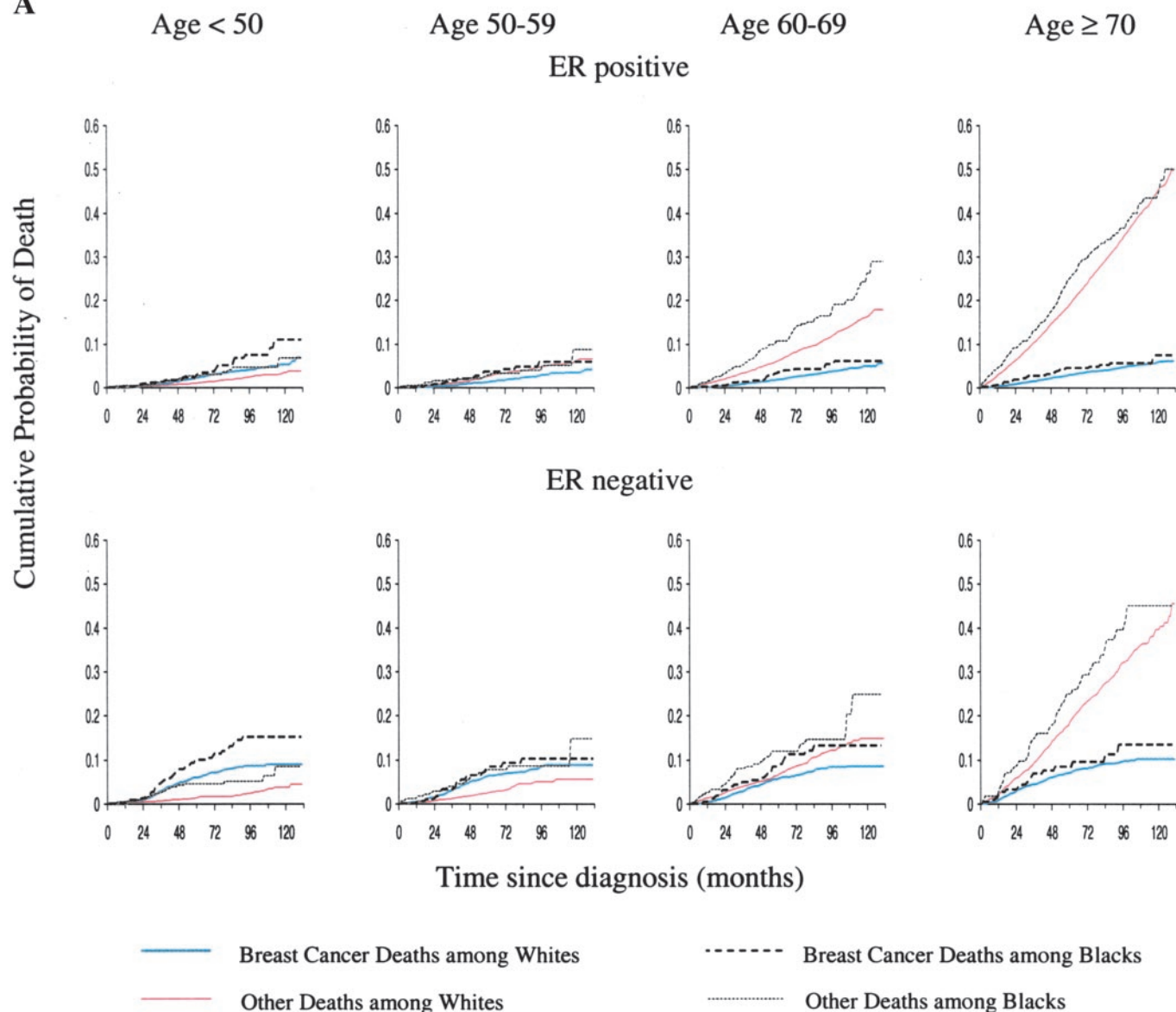
## DISCUSSION

In a competing-risk analysis, we calculated crude cumulative probabilities of death from breast cancer and other causes according to stage, race, and age at diagnosis among 430 510 patients with incident breast cancer in the SEER database diagnosed from January 1, 1973, to December 31, 2000. For patients diagnosed from January 1, 1990, to December 31, 2000, we also calculated probabilities of death according to tumor size and ER status for localized disease

and according to ER status for regional disease. As expected, the probability of death from breast cancer increased with advancing stage; after nearly 28 years of follow-up, it ranged from 0.03 to 0.10 for patients with *in situ* disease to 0.70 to 0.85 for patients with distant disease, depending on race and age. The probability of death from breast cancer was also greater for patients with ER-negative than ER-positive tumors and for patients with larger than smaller tumors. Among patients with known ER status, the probability of death from breast cancer after nearly 11 years of follow-up ranged from 0.04 to 0.11 for patients with localized ER-positive tumors of 2 cm or less to 0.37 to 0.53 for patients with regional ER-negative tumors.

The importance of death from breast cancer versus other causes varied with stage and age at diagnosis. In both white and black patients, the probability of death from breast cancer exceeded the probability of death from all other causes for nearly 28 years after diagnosis among women diagnosed with localized disease (without regard to tumor size or ER status) before age 50 years, with regional disease (without regard to ER status) diagnosed before age 60 years, and with distant disease at any age. For most of the follow-up period, breast cancer was also the predominant cause of death in women diagnosed with regional disease between the ages of 60 and 69 years. For each stage except *in situ* disease, the probability of death from breast cancer at the end of the nearly 28-year follow-up period generally declined with increasing age.

A



**Fig. 2.** Cumulative probability of death from breast cancer and other causes among breast cancer cases with localized disease according to estrogen receptor (ER) status, race, and age at diagnosis (in years), Surveillance, Epidemiology,

and End Results (SEER) Program, 1990–2000. A) Tumors 2 cm or less in diameter. (Continued on facing page).

To our knowledge, this is the first comprehensive competing-risk analysis to quantify the probability of death from breast cancer and other causes after a diagnosis of breast cancer. A previous competing-risk analysis of SEER cases with regional disease also showed a decline in breast cancer mortality with age by the end of the follow-up period (2). Several reports have also shown that other causes of mortality play a greater role in elderly patients (3,7,9,14). Analyses of 5- to 8-year relative survival, however, do not show declines in breast cancer mortality with increasing age at diagnosis (1,7,15).

Older age is viewed as a barrier to receiving aggressive treatment of breast cancer (7,16–18) because the absolute effect of breast cancer mortality on survival diminishes with increasing age as comorbidity from other causes increases (19). In addition, treatment-associated risks, such as complications after surgery and chemotherapy-associated toxicity, have been associated with age-related comorbidity (20,21). In

fact, some data show that older patients receive less aggressive treatment even after accounting for comorbidity (16,17). Our data, however, suggest that death from breast cancer remains a substantial concern, particularly within 5 years after diagnosis, even among older women. These statistics may be particularly relevant in weighing the use of adjuvant chemotherapy in elderly women (6).

Our results are consistent with those of other analyses showing generally poorer breast cancer survival in black patients than in white patients, even after accounting for stage at diagnosis (8,22–25). In one study (8), adjusting for comorbidity slightly reduced the disparity in death from all causes, but not breast cancer, in black patients compared with that in white patients. In our analysis, the higher probability of death from breast cancer among black patients than among white patients with localized or regional disease cannot be attributed to a lower burden of death from other causes; in fact, in



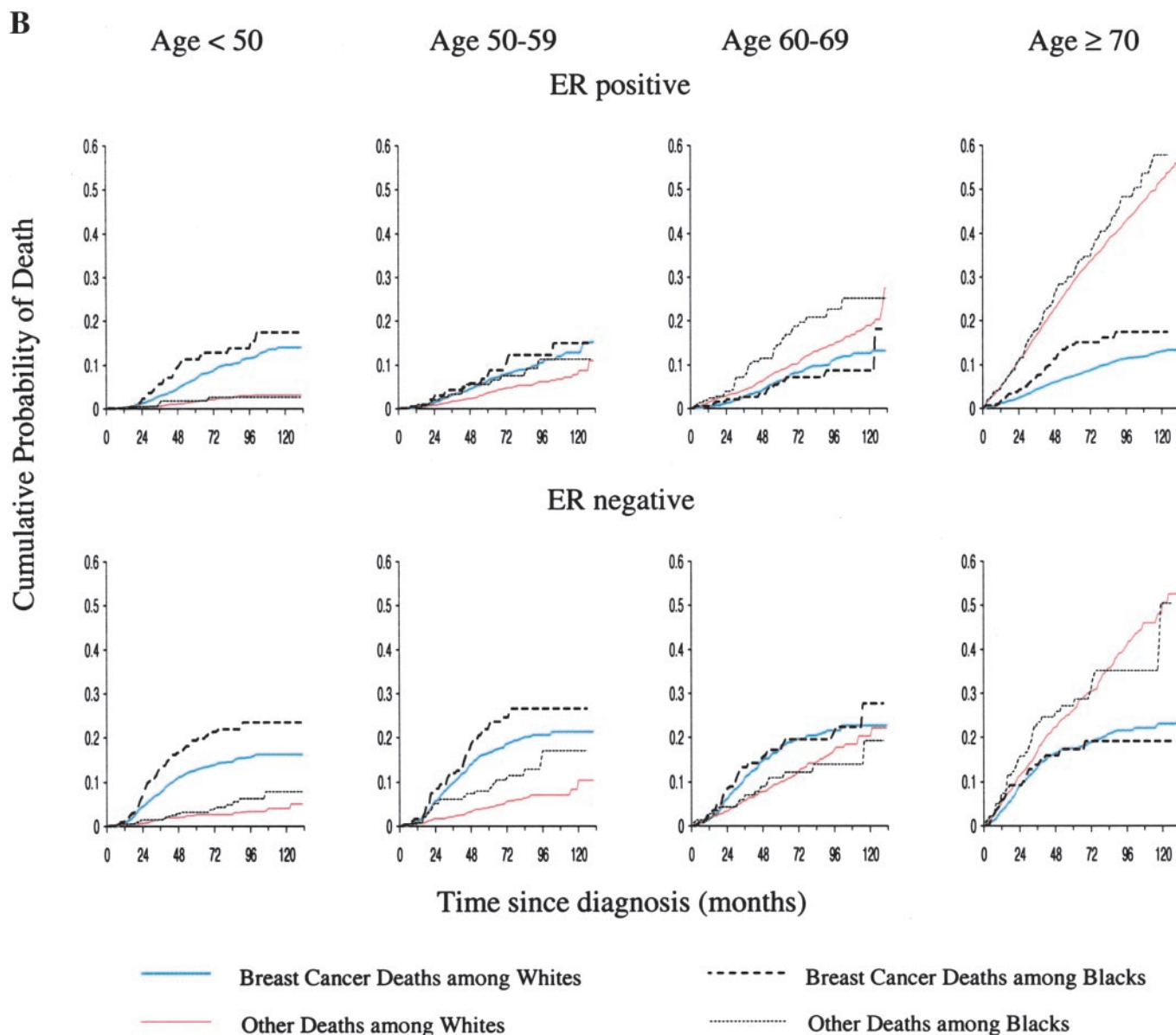


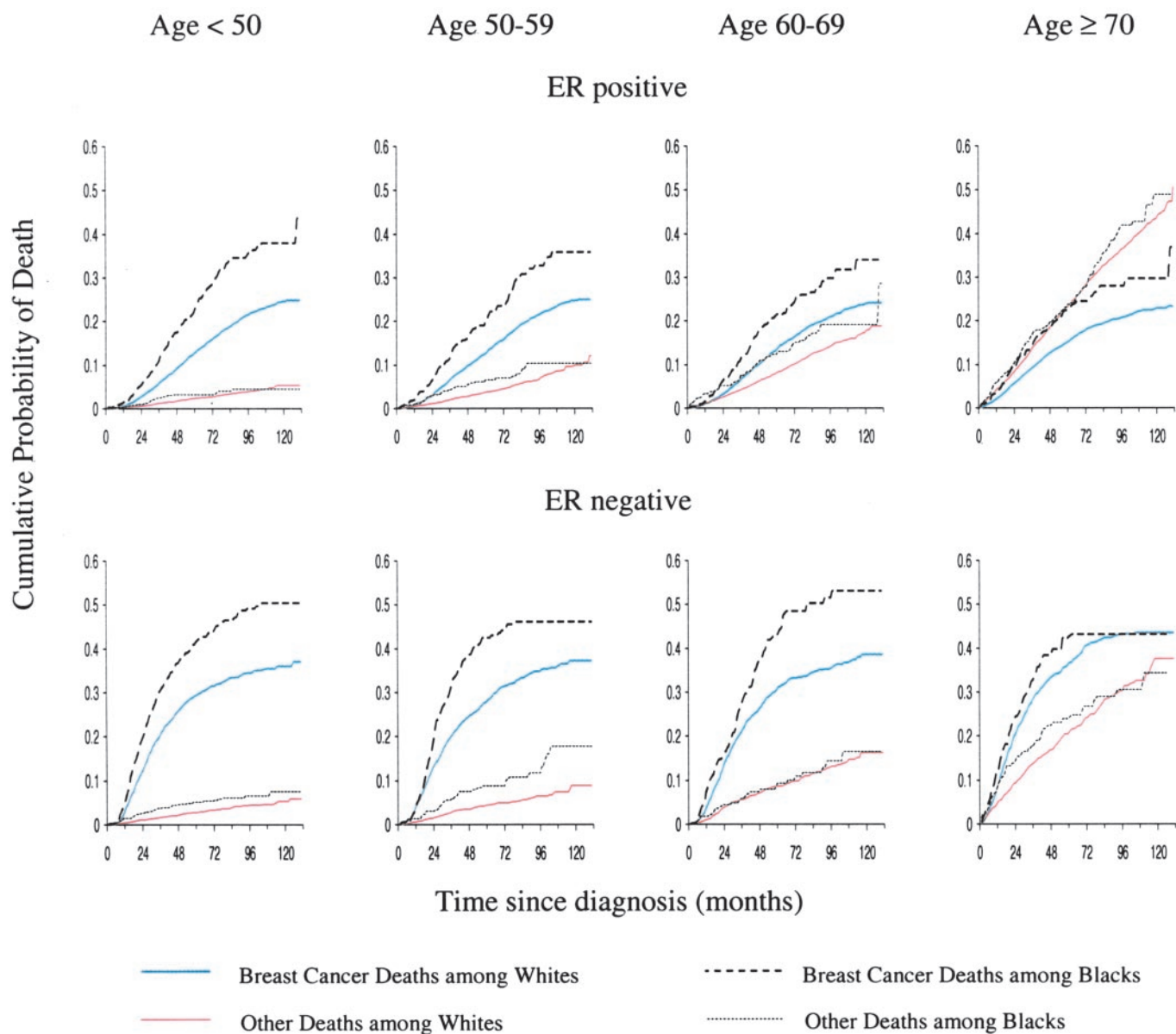
Fig. 2. (Continued from facing page). B) Tumors more than 2 cm in diameter.

these groups, the probability of death from other causes was statistically significantly greater in black patients than in white patients diagnosed before age 70 years. Racial differences in treatment, particularly the lower receipt of radiation therapy after breast-conserving surgery in black patients (26) and more adverse prognostic factors within stage (27), may contribute to the higher breast cancer mortality in black patients than in white patients. The higher probability of death from breast cancer and other causes among black patients than among white patients may also be attributed, in part, to the higher prevalence of obesity and obesity-related morbidities among black patients (28–30).

Our study had several limitations. We did not have information on all breast cancer prognostic factors. Extent of disease, tumor size, and ER status, however, are among the most important prognostic factors for breast cancer survival (31). In fact, axillary lymph node status has been shown consistently to be the single most important predictor of survival (31). By use of SEER

data on nodal status for cases diagnosed from January 1, 1988, to December 31, 2000, we estimate that at least 92% of white and black patients with regional disease had positive lymph nodes. Those with localized disease, of course, had negative lymph nodes. With regard to risk factors for other causes of death, we had information on age only. Thus, our results represent a combination of those both with and without other comorbid conditions.

We also did not have information on treatment received. Our analysis covered a nearly 28-year period during which relative survival has generally increased (1). Thus, the probability of death from breast cancer diagnosed many years earlier reflects treatment patterns and mortality from those earlier periods when relative survival was not as high, but these data remain relevant to women diagnosed during those time periods. In the analyses without regard to tumor size, the short-term probabilities of death from breast cancer reflect patterns of mortality from both earlier and later time periods. We also present results for local-



**Fig. 3.** Cumulative probability of death from breast cancer and other causes among breast cancer cases with regional disease according to estrogen receptor (ER) status, race, and age at diagnosis (in years), Surveillance, Epidemiology, and End Results (SEER) Program, 1990–2000.

ized and regional disease diagnosed from January 1, 1990, through December 31, 2000, a period in which relative survival increased only slightly (*1*).

The accuracy of cause-of-death coding is of potential concern, but a comparison of cause-of-death information on the death certificates with autopsy findings in Connecticut revealed that neoplasms were more accurately diagnosed than other causes of death, with a sensitivity of 87% and a positive predictive value of 85% (*32*). Moreover, the percent agreement of cancer deaths with the original microscopically confirmed diagnosis in the SEER data has been reported to be very high for breast cancer (98.7%) (*33,34*). In one analysis of the accuracy of death certification for cancer of the breast in England, deaths from breast cancer were underestimated by about 4% (*35*). Cancer mortality should include deaths from

cancer treatment, but there is some evidence that treatment-related deaths are not always attributed to the cancer. By use of data from the SEER program, misattribution of deaths within 1 month of breast cancer surgery to other causes of death rather than to breast cancer led to a 0.51% undercount of breast cancer mortality (*36*).

In summary, the probability of death from breast cancer relative to the probability of death from other causes generally declined with age within stage and increased with advancing stage of disease, regardless of age, in both white and black patients. Although death from other causes became increasingly important with advancing age, death from breast cancer remained substantial within the first 5 years after diagnosis, particularly with advancing stage, even among the 33% of white patients and 23% of black patients diagnosed at age 70 years or

older. Finally, the probability of death from breast cancer or other causes in black patients frequently exceeded that in white patients.

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## NOTES

<sup>1</sup>*Editor's note:* SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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